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“Formulation, Development and Evaluation of Niosomes Containing Herbal Extract for Antibacterial and Anticancer activity.”

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ABSTRACT OF PROPOSED WORK PLAN

Herbal remedies have been used to treat various diseases since ancient times due to their high therapeutic potential and less side effects. The extraction, processing, standardization, and identification of herbal medications are difficult. But some inspired scientists develop delivery systems for herbal medicines. Herbal medicines diminished efficacy is because of the outmoded and traditional way in that they are given to patients. The traditional drug delivery systems are dwindling because of less therapeutic effect and higher side effects. To solve such problems, plant medications are now delivered through novel drug delivery techniques like niosomes. In new delivery strategy, herbal medicines will become more efficient and safe as well as extra stable. Niosomes considered as novel drug delivery systems, can improve the solubility and stability of natural pharmaceutical molecules. Niosomes are non-ionic surfactant vesicles which are obtained by hydration of synthetic non-ionic surfactants, cholesterol or other lipids. They are vesicular drug delivery systems similar to liposomes which can be used as carriers of amphiphilic and lipophilic drugs. Niosomes are less toxic and improves the therapeutic index of drug by restricting its action to target cells. Literature data reveals about the various types of herbal niosomal preparations, uses and their results with the Improving accessibility of futuristic natural methods to overcome diseases with herbal niosomes. Using new drug delivery system like niosomes are helpful in herbal formulations with minimizing toxic effect and increasing therapeutic effects. The aim of present study is formulation, development and evaluation of therapeutic potential of herbal niosomes.

Key words: Herbal remedies, novel drug delivery, niosomes, herbal extract, and therapeutic potential

INTRODUCTION

Traditional medicine, still widely practiced today, is rooted in the use of natural substances derived from plants, commonly known as "herbal drugs." With advancements in science and technology, particularly in drug formulation, herbal dosage forms have evolved from basic mixtures and pills to sophisticated, technology-driven drug delivery systems. As the demand grows to minimize the side effects of allopathic medicine, there is increasing interest in developing herbal formulations using innovative drug delivery systems, such as niosomal formulations. Herbal medicines, sourced from plants, provide therapeutic or other beneficial effects for humans. For thousands of years, natural products especially plants have been used to treat a wide range of ailments, with many modern pharmaceutical drugs being derived from these plant-based compounds. These plants can be sold either in their raw form or as extracts, where the plant material is processed with solvents like water, alcohol, or others to isolate bioactive compounds including fatty acids, sterols, alkaloids, flavonoids, glycosides, saponins, and more.[1]

Niosomes are an advanced drug delivery system that can encapsulate both hydrophilic and hydrophobic drugs. Hydrophilic drugs are trapped in the core cavity, while hydrophobic drugs are incorporated into the non-polar regions of the bilayer, allowing for the simultaneous incorporation of both types of drugs [2]. Niosomes are amphiphilic in nature, where the medication is encapsulated within a vesicle made from nonionic surfactants, which gives rise to the name "niosomes." These vesicles are extremely small and microscopic in size [3]. The first niosome formulations were developed and patented by L'Oréal in 1975. With the right mixture of surfactants and charge-inducing agents, niosomes form thermodynamically stable vesicles. Niosomes are primarily studied as alternatives to liposomes due to their ability to address some of the disadvantages of liposome [4]. One key advantage of niosomes is their ability to overcome the chemical instability commonly associated with liposomes, which are prone to oxidative degradation and may suffer from variable purity of phospholipids. The main goals of developing niosomal systems include enhanced chemical stability, biodegradability, biocompatibility, low production costs, ease of storage and handling, and low toxicity [5,6].

Niosomes can be administered through various routes, including oral, parenteral, and topical. They serve as effective delivery systems for a wide range of drugs, including synthetic and herbal medicines, antigens, hormones, and other bioactive compounds [7,8,9]. Niosomes can be

utilized in the treatment of several diseases like Psoriasis, leishmaniasis, cancer, migraine, Parkinson etc. Niosomes can be used as diagnostic aid. Various methods of niosomal administration include intramuscular, intravenous, oral and transdermal. Niosomal technology is widely used in cosmetics. Still researchers have to focus a lot on the commercial utility of niosomes in drug delivery. [10]

Niosomal formulations offer a promising approach for delivering various anticancer drugs with reduced side effects. Unlike conventional chemotherapy, which lacks the ability to selectively target cancerous cells, niosomes provide both passive and active drug delivery to tumor tissues. Traditional chemotherapy is associated with low therapeutic efficacy, significant toxicity to healthy cells, and a high incidence of side effects. Niosomal drug delivery systems can overcome issues such as low bioavailability, poor stability, and limited access to drugs due to the blood-brain barrier's low permeability. Studies have shown that niosomal formulations can reduce the toxicity of compounds like Withaferin-A (WA) from *Withania somnifera*, tamoxifen (TMX)/curcumin, and curcumin itself.

Niosomes utilize various release mechanisms for targeting cancer cells, including temperature, light, pH, enzymatic degradation, and ultrasound activation of bilayer vesicle breakdown. For example, alginate-coated niosome-based nanocarriers have been developed to co-deliver doxorubicin (Dox) and cisplatin (Cis) for breast and ovarian cancer treatment, showing promising results. Additionally, a new nano-drug delivery platform using niosomal formulations of curcumin, coated with a chitosan polymeric shell and combined with Rose Bengal (RB), a photosensitizer with antibacterial properties, demonstrated significant anticancer and antibacterial effects against Gram-negative bacteria and lung cancer cells.

Novel formulation that includes doxorubicin-loaded, pH-responsive stealth niosomes with CdSe/ZnS quantum dots for imaging, highlighting its potential for cancer theranostic applications are invented. Furthermore, various niosomal formulations were shown to significantly reduce the expression of genes associated with metastasis, such as COL10A1, MMP2, and MMP9. These formulations also exhibited strong anti-proliferative activity by inhibiting anti-apoptotic genes and promoting apoptotic gene expression in A549 lung cancer cells. The following sections discuss recent in-vitro and in-vivo studies on anticancer drug-loaded niosomes, highlighting some remarkable results from these research efforts. [13]

Salient Features of Niosomes: [11,12]

- Niosomes have the ability to encapsulate solutes, enhancing the solidification of the encapsulated drug due to their osmotic stability under diverse conditions.
- Niosomes are composed of non-ionic surfactants that are safe, non-immunogenic, and biodegradable.
- The structure of niosomes is predominantly hydrophobic and deliquescent, facilitating the encapsulation of drug molecules with a wide range of solubility profiles.
- Niosomes are particularly effective for the delivery of labile and sensitive pharmaceutical compounds.
- By shielding the drug from its external biological environment, niosomes enhance the drug's targeted availability at the desired site of action.

Advantages of Niosomes: [1]

- Minimized adverse effects and exhibits the longest possible action.
- The preparation's active ingredient or constituent is shielded by a bilayer from various external and internal variables.
- The vesicles can act as a depot to release the drug slowly and offer a controlled release
- Niosomes can be administered parenterally, topically, or orally.
- Non-ionic surfactants in niosomes can act as penetration enhancers various niosome preparation techniques have been used due to their ability to fluidize the stratum corneum lipid reported and it has been found that niosomal properties bilayers and diffuse through them.

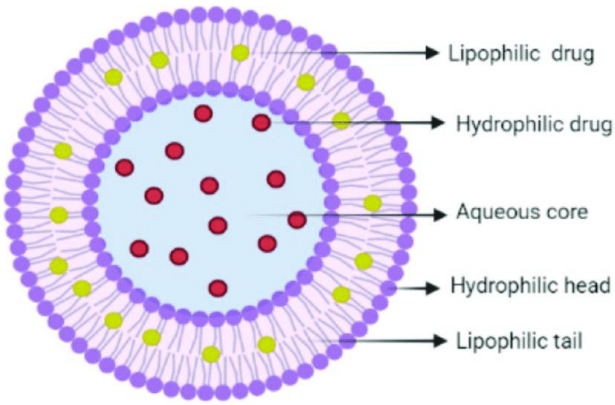

Figure 1: General structural representation of niosomes.

Composition of Niosomes [12,13]**:**

Ingredient	Use	Example
Non-ionic surfactants	Surface active agent main ingredient	• Alkyl esters: Span and Tween • Alkyl amides: Galactosides, Glucosides • Alkyl ethers: Brij • Esters of fatty acids: Glycerol Monosterate • Bola surfactants: Bola 16 • Gemini surfactants: Sodium dilauramidoglutamide lysine(DLGL) • Bio surfactants: Mannosyl erythritol lipid-B(MEL-B)
Cholesterol	provide rigidity, proper shape and conformation increases the entrapment efficiency	Cholesterol
Charge inducer	Increases the stability by electrostatic repulsion to avoid coalescence	positive charge inducers: stearylamine and cetylpyridinium chloride negative charge inducers: dicetyl phosphates, dihexadecyl phosphate and lipoamide acid
Hydration medium	Enhances solubility of the medicine being encapsulated	Phosphate buffer at different pH

REVIEW OF LITERATURE AND DEVELOPMENT IN THE SUBJECT

Paseban K, *et al* (2024) Various niosome-encapsulated meropenem formulations were prepared to address mutations. Their antibacterial and anti-biofilm activities were tested against methicillin-resistant *Staphylococcus aureus* (MRSA) strains. The physicochemical properties of the niosomal formulations were characterized, and their antibacterial and anti-biofilm effects were evaluated using broth microdilution and minimum biofilm inhibitory concentration (MBIC) methods. [16]

Saharkhiz S, *et al* (2023) A novel smart nano-platform has been developed, consisting of doxorubicin-loaded, pH-responsive stealth niosomes incorporating CdSe/ZnS quantum dots as imaging agents. The drug-loaded nano-platform was fabricated using the thin-film hydration method and subsequently assessed through various physicochemical tests. This innovative nanoformulation demonstrates promising potential for future cancer theranostic applications. [17]

Zarepour A, *et al* (2023) A new smart nano-drug delivery system has been developed with both antibacterial and anticancer properties, designed for the treatment of lung cancer. This system features a niosomal carrier encapsulating curcumin as the anticancer agent, coated with a chitosan polymeric shell. Additionally, it incorporates Rose Bengal (RB) as a photosensitizer, providing antibacterial capabilities. [18]

Sefidan Jadid M, *et al* (2023) Curcumin-loaded niosomal nanoparticles (NPs) were combined with a heat-killed form of *Saccharomyces cerevisiae* as an anti-cancer agent targeting colorectal cancer cells. The curcumin-loaded niosomal NPs (N-Cur) were synthesized using the thin-film hydration method. The synthesized nanoparticles were characterized through techniques such as DLS, FT-IR, SEM, and AFM. The cytotoxicity of these agents and their effects on gene expression were evaluated using the MTT assay and real-time PCR, respectively.[19]

Al-Enazi N, *et al* (2023) In this study, *Pistacia atlantica* fruit extract was loaded onto a new Pluronic vesicular nano platform (Nio) and analyzed using various techniques. This formulation showed increased cytotoxicity against BT-20 and MCF-10 cell lines compared to the extract alone, suggesting its potential as a drug carrier with prolonged release properties. Additionally, the Nio/Extract combination displayed stronger antibacterial effects against Pseudomonas aeruginosa, Staphylococcus epidermidis, and Candida albicans.[20]

Haddadian A, *et al* (2022) In this study, SeNPs were synthesized using a green synthesis method with *T. cherleri* extract. Their characterization included size, morphology, crystallinity, and the percentage of SeNPs. Additionally, SeNPs were loaded into niosomes for the first time, and their biological effects, including antibacterial, anti-biofilm, and anti-cancer activities, were studied.[21]

Cetin E, *et al* (2022) *Propolis* (bee glue) is a promising candidate for cancer treatment due to its ability to target various tumor cells and its broad spectrum of biological and pharmacological activities, which arise from the diversity of its components. This study utilized both 2D and 3D cell cultures to compare the antitumorigenic properties of ethanol extract of propolis (EEP) and propolis-loaded niosomes (PLN). Niosome formulations were prepared using the thin-film hydration method. Niosomes are effective pharmaceutical delivery systems in cancer therapy, benefiting from the enhanced permeability and retention (EPR) effect, which allows nanoparticulate systems to accumulate more in cancer cells.[22]

Sirati R, *et al* (2022) Researchers aimed to explore the use of niosomes as a delivery system to enhance the effectiveness of oregano essential oil against food-borne pathogens. They examined the structural and morphological properties of various niosome formulations. The antimicrobial and anti-biofilm effects of niosomes containing oregano essential oil were tested using the microbroth-dilution and microtiter-plate methods. Additionally, the biocompatibility of the synthesized niosomes was assessed using the MTT method on a human foreskin fibroblast (HFF) normal cell line.[23]

Sanghadeep, G, *et al* (2022) *Taraxacum officinale*, commonly known as dandelion, is a weed typically found growing along roadsides, in crops, and other wild areas. It belongs to the Asteraceae family. Both the roots and leaves of the plant possess a variety of potential health benefits, including hepatoprotective, antioxidant, blood sugar-lowering, and triglyceride and cholesterol-reducing activities. Traditionally, dandelion has been used as a diuretic for many years. It is rich in potassium and multivitamins, and is also utilized in managing hypertension and lowering blood pressure. The primary bioactive constituents in dandelion, such as beta-carotene and polyphenols, are known for their pharmaceutical potential. These compounds can be developed into phytosomes to enhance the bioavailability and solubility of dandelion extract, although they are not typically present in the plant extract preparations.[24]

Swetha V, *et al* (2021) Herbal niosomes for wound healing were developed using a Soxhlet apparatus to extract *Psidium guajava*. The extract was analyzed for its phytochemical properties, antimicrobial activity, and thin-layer chromatography (TLC) profile. Various parameters, such as drug concentration, entrapment efficiency, particle size, zeta potential, and in-vitro drug release, were evaluated. The developed formulation shows promising potential for wound healing applications.[25]

Moghaddam F, *et al* (2021) A melittin-loaded niosome was developed for breast cancer treatment. It shows better targeting, higher encapsulation efficiency, improved PDI (polydispersity index), and faster release rate. The treatment also has a strong anticancer effect on cell lines. It increases the rate of cell death (apoptosis) and reduces cell migration and invasion in both cell lines, compared to melittin alone. Histopathology results showed a lower mitosis index, less invasion, and reduced pleomorphism in the melittin-loaded niosome samples.[26]

Moghtaderi M, *et al* (2021) Highlight the urgent need for alternatives to traditional antibiotics due to the increasing prevalence of antibiotic-resistant bacteria. Among the promising solutions are medicinal plant extracts, which contain bioactive compounds. The study focuses on preparing niosome-encapsulated Echinacea angustifolia (coneflower) extract and evaluating its effectiveness against multidrug-resistant strains of *Klebsiella pneumoniae*. A Design of Experiments approach was used to optimize the encapsulation process before conducting experimental research. The encapsulated E. angustifolia extract exhibited up to 16 times greater antibacterial activity against multidrug-resistant *K. pneumoniae* strains compared to the free extract.[27]

Shyamala G, *et al* (2021) investigated the traditional use of *Psidium guajava* (guava) and *Justicia adhatoda* (Malabar nut) leaves in Indian herbal medicine for treating dengue. The study aimed to evaluate the antiviral activity of phyto-niosomes (PN) loaded with aqueous extracts of guava (PG) and Malabar nut (JA) against the dengue virus-2 (DEN-2) strain. Based on its safety, effectiveness, and mechanism of action, the formulation could potentially be used for dengue treatment following clinical trials.[28]

Akbarzadeh I, *et al* (2020) Doxycycline-loaded niosomes exhibit both antibacterial and anti-cancer effects, making them valuable for treating infection-associated cancers, particularly prostate cancer. The antibacterial properties of doxycycline-loaded niosomes were assessed against various Gram-negative and Gram-positive bacteria, showing a significant reduction (50 -75%) in MIC

values. Additionally, the niosomal formulation demonstrated promising chemotherapy effects against prostate cancer cells (PC3), while also enhancing biocompatibility with normal HEK293 cells.[29]

Barani M, *et al* (2019) For herbal cancer treatment, two different formulations containing *Thymoquinone* (TQ) and *Carum* were encapsulated into niosomes (Nio/TQ and Nio/Carum). Their properties were compared. The evaluations included morphology, size, zeta potential, encapsulation efficiency (EE%), release rate profile, in vitro cytotoxicity, cytometric analysis, DNA fragmentation, and cell migration assays.[30]

Morakul B, *et al* (2019) Pumpkin seed oil (*Cucurbita pepo* L) (PSO) offers numerous health benefits, including antioxidant properties, support for cardiovascular health, treatment of benign prostatic hyperplasia, and prevention of hair loss. In this research an effective niosomal formulation was developed for the topical delivery of PSO.[31]

Mahdie H, *et al* (2018) Formulated and optimized the cationic PEGylated niosome-containing anti-cancer drugs and siRNA to enhance the therapeutic response. Therefore, various surfactant-based (tween-60) vesicles of doxorubicin (DOX; a chemotherapeutic drug) and quercetin (QC; a chemosensitizer) were prepared. Additionally, noiosome-encapsulated drugs had a higher toxicity against cancer cells when compared with un-encapsulated forms and the synergistic effects of co-delivery of siRNA and DOX with QC on gastric, prostate, breast cancer cells as well as human foreskin fibroblast as a normal cell line was shown. The results showed that the co-delivery of drugs and siRNA using cationic PEGylated niosomes exhibited an increased anti-cancer activity against the tumor cell death. It seems that cationic PEGylated niosomes have opened up a new avenue to enrich the armamentarium of therapeutic agents to fight cancer.[32]

Agarwal S, *et al* (2018) Morusin, a water-insoluble flavonoid derived from the root bark of *Morus alba* (white mulberry), possesses various medicinal properties, including anti-inflammatory, antioxidant, and antibacterial activities. It also suppresses genes involved in tumor progression. However, due to its poor solubility, morusin suffers from low bioavailability and rapid degradation, limiting its clinical applications. To address this issue, a niosomal formulation was developed to enhance its aqueous solubility. The thin-film evaporation technique was slightly modified to prepare morusin-loaded niosomes. These niosomes provided steady and sustained drug release, with increased release at acidic pH, suggesting effective drug release in the acidic environment of

cancer cells. The controlled and sustained release of morusin enhanced its therapeutic efficacy in the evaluated cancer cell lines.[33]

Kassem M, *et al* (2017) imatinib mesylate (IM)-loaded niosomes to improve its chemotherapeutic efficacy. The influence of 3 formulation factors on niosomal vesicular size (Y_1), zeta potential (Y_2), entrapment capacity percentage (Y_3), the percentage of initial drug release after 2 h (Y_4), and the percentage of cumulative drug release after 24 h (Y_5) were studied and optimized using Box-Behnken design. Optimum desirability was specified and the optimized formula was prepared, stability tested, morphologically examined, checked for vesicular bilayer formation and evaluated for its *in vitro* cytotoxicity on 3 different cancer cell lines namely MCF-7, HCT-116, and HepG-2 in addition to 1 normal cell line to ensure its selectivity against cancer cells.[34]

Sharma P, *et al* (2017) Lycopene, a principal carotenoid found in ripe tomatoes (*Lycopersicum esculentum*), is responsible for the characteristic red color of the fruit and has attracted attention for its potential health benefits. Liposomes, while useful, faces stability issues such as aggregation, fusion, leakage, and sedimentation during storage. Niosomes, which are non-ionic vesicles made from cholesterol and surfactants, can address these issues. These vesicles offer enhanced stability and solubilization, improving the bioavailability of active compounds like lycopene in aqueous intestinal secretions. Nonionic surfactants, similar to phospholipids, enable the formation of niosomal systems when dispersed in aqueous solutions, providing a promising alternative for drug delivery.[35]

Wolfle U, *et al* (2014) A niosomal topical gel was developed using *Hypericum perforatum* (St. John's Wort), incorporating known amounts of phloroglucinols, naphthodianthrones, and polyphenolic compounds. This gel utilized a successful transdermal drug delivery system capable of entrapping both lipophilic and hydrophilic constituents for wound and scar treatment, prepared through the reverse phase evaporation method. Assuming the synergistic action of hyperforins, hypericins, flavonoids, and phenolic compounds, the niosomal gel containing 1.5% sodium carboxymethylcellulose demonstrated strong wound-healing effects in 16 adult mongrel dogs, outperforming panthenol in efficacy.[36]

RESEARCH GAPS

1. **Development of Niosomal Formulations:** There is a need to explore and optimize the formulation of niosomes with herbal extracts, leveraging their advantages over conventional and other vesicular drug delivery systems.

2. **Synergistic Effects of Herbal Combinations:** Limited research exists on the combination of different herbal extracts in niosomes to evaluate their potential additive or synergistic effects for enhanced therapeutic outcomes.

3. **Surfactant Combinations for Stability:** Further studies are needed to investigate the use of various surfactant combinations to achieve more stable and efficient niosomal formulations.

4. **Infections Associated with Cancer Treatment:** While niosomes have shown promise in providing antibacterial and anticancer effects, more research is required to fully explore their potential in treating infection associated with cancers.

5. **Limited In-Vivo Studies:** Most studies on herbal niosomes are restricted to in-vitro experiments (cell cultures, enzyme studies), and there is a significant gap in comprehensive in-vivo studies evaluating the therapeutic potential, safety, and toxicity of herbal niosomes.

6. **Herbal Niosomes for Cancer Therapy:** There is a lack of extensive research on the application of herbal niosomes in cancer therapy, especially for their ability to improve drug delivery, bioavailability, targeted delivery, and controlled release.

7. **Formulation of Combined Antibacterial and Anticancer Herbal Niosomes:** There is a need for formulating herbal niosomes that combine both antibacterial and anticancer effects and conducting in-vitro studies to assess their therapeutic potential in cancer treatment.

AIM & OBJECTIVES OF RESEARCH

Aim: Formulation development and evaluation of niosomes containing herbal extract for antibacterial and anticancer activity.

Objectives of Research/ Proposed Hypothesis:

The objectives of present study are given below:

1. To prepare medicinal plant extract, its physicochemical characterization and quanification of bioactive content.

2. Optimization of formulation using Design of Experiments approach.

3. To formulate niosomes of extract using non-ionic surfactant, cholesterol etc. by using suitable method.

4. To carry out evaluation study as vesicle size and shape analysis by using SEM and TEM, Drug content, Percentage of entrapment efficiency, in-vitro drug release, etc.

5. To formulate & evaluate suitable dosage form for targeted delivery of bioactive constituent.

RESEARCH HYPOTHESIS:

"The formulation of niosomes incorporating plant extracts with anticancer and antibacterial properties enhances the stability, controlled release, and therapeutic efficacy of the active compounds compared to conventional formulations."

Research Approach:

1. **Literature Review**

   Conduct a thorough review of existing literature on plant extracts with anticancer and antibacterial activity. This will help in selecting appropriate plants and understanding the background on niosomal drug delivery systems, their benefits, and limitations.

2. **Selection and Collection of Plant & Excipients**

   - Plants: Select plants known for their proven anticancer and antibacterial properties
   - Excipients: Choose surfactants like Span 20, 40, 60, 80, Tween 20, 40, 60, 80, which are essential for forming stable niosomes.
   - Other Chemicals: Collect necessary chemicals like cholesterol (for membrane stability), triethanolamine (for charge and stability), ethanol, methanol (as a solvent), chloroform (for extraction), etc.

3. **Preparation of Extract Using Suitable Solvent**

   The plant extract will be prepared using a suitable solvent system, such as ethanol or methanol, to ensure maximum extraction of bioactive compounds (anticancer and antibacterial agents).

4. **Phytochemical Evaluation**

   Analyze the phytochemical composition of the plant extracts to identify the presence of active compounds (e.g., alkaloids, flavonoids, tannins, terpenoids), which contribute to the anticancer and antibacterial activities and quantification of bioactive content by using various instrumental techniques e.g. HPLC, UV, GC-MS, TLC.

5. **Acute Toxicity Studies**

   Perform acute toxicity studies of the plant extracts to ensure their safety before incorporating them into niosomal formulations.

6. **Formulation Development**

   - Optimize the formulation by using Design of Experiment software using the variables like concentration of surfactants, cholesterol, and other excipients.

- Preparation of Niosomes: Use a suitable method (e.g., thin-film hydration method, reverse-phase evaporation) to prepare niosomes loaded with the plant extract.

7. Evaluation of Prepared Niosomes

- Appearance: Observe the physical appearance for uniformity and clarity.
- pH: Measure the pH to ensure compatibility with biological membranes.
- Vesicle Size & Shape Analysis: Use Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) to analyze the vesicle size, shape, and morphology.
- Drug Content: Quantify the drug content to ensure the correct amount of bioactive compounds are encapsulated.
- % Entrapment Efficiency: Determine the efficiency of encapsulation using centrifugation or dialysis method.
- Stability Studies: Conduct stability studies under different conditions (e.g., temperature, humidity) to assess long-term stability.
- In-vitro Drug Release: Use a suitable in-vitro model (e.g., dialysis method) to evaluate the controlled release of the active ingredients from the niosomes.

8. Formulation of Dosage Form

Develop the final dosage form, such as suspensions, lyophilized (freeze dried) powder incorporating the prepared niosomes.

9. Evaluation of Dosage Form

- Assess the dosage form for physical stability, homogeneity, drug content, and release kinetics.

IMPORTANCE OF STUDY

Rational of Study: The increasing prevalence of cancer and infection-related complications has led to a growing demand for more effective treatment options that minimize the adverse effects associated with conventional allopathic medicines. While synthetic drugs have proven effective in treating various cancers and infections, they often come with significant toxicities, affecting the patient's quality of life. Herbal remedies, with their therapeutic potential and fewer side effects, have emerged as viable alternatives. However, traditional herbal formulations often suffer from issues related to poor bioavailability, instability, and low efficacy due to inadequate delivery mechanisms.

Niosomes, non-ionic surfactant vesicles, have shown significant promise as advanced drug delivery systems for improving the stability, solubility, and controlled release of therapeutic agents. These vesicles, which can encapsulate both lipophilic and hydrophilic substances, provide a targeted and efficient means of delivering active compounds, enhancing their therapeutic effects while reducing toxicity. In particular, niosomes have demonstrated notable antibacterial and anticancer activities, making them a valuable tool in the treatment of infection-associated cancers.

The rationale behind this study is to formulate and evaluate herbal niosomes that combine both antibacterial and anticancer properties, leveraging the synergistic effects of herbal compounds. By incorporating these bioactive herbal ingredients into niosomal formulations, it is possible to achieve better targeted delivery to cancerous tissues while simultaneously combating infection-related complications. The study will explore the formulation of these combined herbal niosomes, assess their in-vitro efficacy, and investigate their potential to provide a safer, more effective alternative to traditional treatments. This innovative approach aims to enhance therapeutic outcomes, minimize side effects, and pave the way for the development of safer, plant-based treatment options for cancer and infection.

National Status:

In India, herbal medicine has long been a cornerstone of healthcare, with increasing interest in using natural remedies to address the side effects of synthetic drugs, particularly in cancer and infection treatments. While traditional herbal formulations face challenges such as poor bioavailability and stability, innovative drug delivery systems like niosomes are being explored to overcome these limitations. Niosomes, which improve the solubility, stability, and targeted delivery

of herbal compounds, are gaining attention for their potential in enhancing the therapeutic effects of herbal medicines. Indian research institutions and pharmaceutical companies are actively developing herbal niosomes with antibacterial and anticancer properties. Supported by government bodies like the Department of Biotechnology (DBT) and Indian Council of Medical Research (ICMR), this field is progressing rapidly, aiming to offer safer, more effective alternatives to conventional treatments.

International Status:

Globally, there is a growing interest in developing advanced drug delivery systems like niosomes to enhance the efficacy and safety of herbal medicines. Research on niosomes has gained significant attention due to their ability to improve the solubility, stability, and targeted delivery of therapeutic agents, including herbal compounds. Niosomes are being explored for a wide range of applications, including the treatment of cancer, infections, diabetes, and other diseases. International studies, particularly in cancer research, have demonstrated the potential of niosomal formulations in enhancing the bioavailability and therapeutic effects of phytochemicals. The combination of herbal medicines with nanotechnology, including niosomes, is recognized as a promising strategy to address the challenges of traditional drug delivery systems. This global trend is supported by increased investment in nanomedicine and ongoing research into the use of herbal niosomes as a safer, more effective alternative to conventional treatments.

Table 1. Natural Products Loaded Niosomes for Pharmaceutical Applications [13]

Niosome Type	Natural Product	Disease Type	Results
LUV	Lycopene	Cervical and breast Cancer	Anti-cancer activity
LUV	Curcumin	Cancer	Multi hydrophilic and hydrophobic drug delivery
LUV	Morusin	Cancer	Anti-cancer activity
LUV	Gambogenic acid	Cancer	Effective release and increasing duration
SUV	Curcumin	Cancer	Improving therapeutic effectiveness of cancer treatments
SUV & LUV	Nerium oleander	Alveolar type-II and cervical cancer cell	Antioxidant activity
SUV	Morin	Cancer and Parkinson	Antioxidant and anticancer activity in brain
LUV	Green tea	Skin Protection	Efficient encapsulation
LUV	Silibin	cancer	Altering level of miRNA expression
SUV	carum	cancer	Novel High efficiency carrier
LUV	Rice Bran	Skin Aging	Skin lightning, thickness, roughness and elasticity improvement
LUV	Lycopene	Diabetus	Efficient delivery. Blood glucose level reduction
SUV	Zingiber	Inflammation	Antioxidant and antiinflammatory
LUV	Embelin	Diabetus	Hypoglycemic activity
LUV	Gymnema sylvestre	Diabetus	Hypoglycemic activity
LUV	Silymarin	Hepatoprotective	Increasing drug bioavailability
LUV	Ellagic acid	Skin disease	Efficient delivery of EA through epidermis
LUV	Ammonium Glycyrrhizinate	Eczema and psoriasis	Skin permeation enhancement
LUV	Resveratrol	Skin inflammation and irritation	Skin permeation enhancement, Preventing trans-to-cis photoisomerization of resveratrol
LUV	Papain	Scar of skin	Skin permeation enhancement
LUV	Aloe vera	Cancer, Skin defects and wounds	Targeted drug delivery

LUV	Ginkgo biloba	Auto-oxidation, antitumor, protective in nervous system	Improved effect
LUV	Artemisia absinthium	Amyloid aggregation	Targeted drug delivery
LUV	Marigold	Cytotoxicity, wound healing, antioxidant	Improved effect
LUV	Zingiber	Anti-inflammatory	Chemical stability and skin permeation enhancement
LUV	Propolis	Oral recurrent aphthous ulcer	Improved effect
LUV	meropenem	antibacterial and anti-biofilm activities	Improved effect
LUV	Pistacia atlantic	Lung cancer	Anticancer
LUV	T. cherleri	Antibacterial, anti-cancer and anti-biofilm	Improved effect
LUV	Propolis	Cancer	Anticancer

PROPOSED WORK PLAN

Sr. No.	Expected target to be achieved	1-6 Months	7-10 Months	11-22 Months	22-27 Months	28-33 Months	34-36 Months
1	Literature survey	Literature survey					
2	Selection and collection of plant and excipients	Selection and collection of plant extract and excipients					
3	Formulation, development and optimization	Formulation, development and optimization					
4	Evaluation	Evaluation					
5	In vitro Study	In vitro study					
6	Statistical Analysis, Data Interpretation and Conclusions	Statistical Analysis, Data Interpretation and Conclusions					
7	Publishing Research and submitting data	Publishing Research and submitting data					

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